NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects of MBG453 with standard treatment in people with certain blood cancers

Thank you!

Thank you to the participants who took part in the clinical trial for certain blood cancers including **myelodysplastic syndrome (MDS)** and **chronic myelomonocytic leukemia (CMML)**. Every participant helped the researchers learn more about the trial drug **MBG453** given with **standard treatment**.

Novartis sponsored this trial and believes it is important to share what was learned from the results of this trial with the participants and the public. We hope this helps the participants understand their important role in medical research.

Trial information

Trial number: CMBG453B12301

Novartis drug studied: **MBG453**, also called sabatolimab

Sponsor: Novartis

If you were a participant and have any questions about the results, please talk to the doctor or staff at the trial site.

This summary only shows the results of a single clinical trial. Other clinical trials may have different results.

What was the main purpose of this trial?

The purpose of this trial was to learn about the effects of **MBG453** given with standard treatment for people with certain blood cancers. **Standard treatment** alone does not always work for everyone with these cancers, so researchers are looking for other ways to treat them. To find this out, researchers compared the effects of **MBG453 with standard treatment** to **placebo with standard treatment**.

The blood cancers in this trial were:

- **Myelodysplastic syndrome (MDS),** which is a group of blood cancers that happen when blood cells don't develop or work properly. This trial focused on types of MDS that were **intermediate, high, or very high risk**. These types of MDS might become acute myeloid leukemia, which is a fast-growing type of blood cancer.
- **Chronic myelomonocytic leukemia (CMML)**, which is a cancer that affects the cells that become blood cells. In CMML, there are too many abnormal white blood cells called monocytes. This trial included CMML at **stage 2**, which means a high number of abnormal white blood cells.

MBG453, also called sabatolimab, is a trial drug created to block a protein called TIM-3. TIM-3 is a protein on some cells in the immune system. TIM-3 can lower the immune system's ability to find and kill cancer cells. By blocking TIM-3, **MBG453** may help the immune system be more active to find and kill cancer cells.

Trial drug
MBG453 also called sabatolimab

Pronounced as
saba-to-li-mab

Standard treatment is azacitidine. **Azacitidine** is a chemotherapy that is approved to treat MDS and CMML in certain countries. **Chemotherapy** is a type of treatment that kills cancer cells or stops them from growing.

A **placebo** looks like the trial drug but does not have any drug in it. Using a **placebo** helps researchers better understand the effect of a trial drug.

The trial's purpose was to answer these main questions:

- Did participants who received MBG453 with standard treatment live longer than those who received placebo with standard treatment?
- What medical problems, also called adverse events, happened during this trial?
  - ↳ An **adverse event** is any sign or symptom that participants have during a trial. Adverse events **may** or **may not** be caused by treatments in the trial.

How long was this trial?

The trial began in June 2020 and ended in October 2024. Each participant was in the trial for up to 4 years.

The trial ended early because the results showed that participants with MDS or CMML who received **MBG453 with standard treatment** did not live longer than those who received **placebo with standard treatment**.

Participants who were receiving **MBG453 with standard treatment** and could benefit from it were given the option to join another trial, **CMBG453B12206B**, to continue to receive **MBG453 with standard treatment**.

Who was in this trial?

530 participants joined this trial – 347 men and 183 women. 492 had MDS and 38 had CMML. Participants' ages ranged from 20 to 94 years. Their average age was 70 years.

The number of participants by race is shown below.

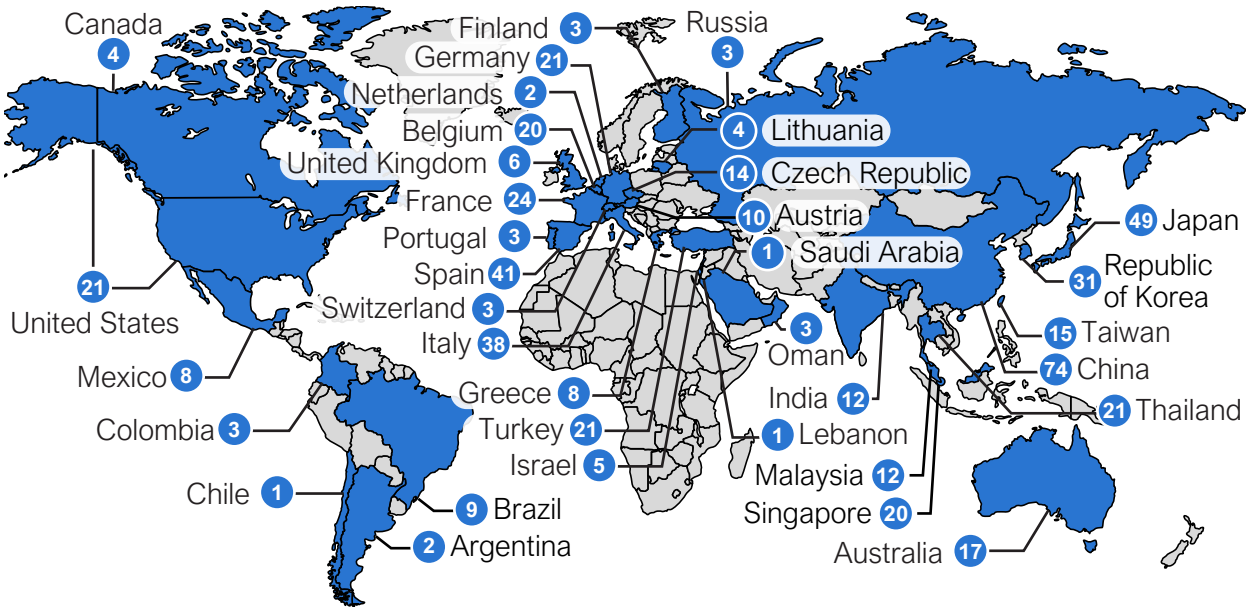
Race

3	American Indian or Alaska Native	235	Asian	7	Black or African American
284	White	1	Unknown		

The participants could take part in this trial if they:

- Had blood cancer that was either:
  - **MDS** that was intermediate, high, or very high risk
  - **CMML** that was stage 2
- Could not receive high dose chemotherapy or a bone marrow transplant at the start of the trial - a **bone marrow transplant** (also called a stem cell transplant) gives blood cells from the bone marrow of a healthy person to a person who needs them
- Did not have another type of blood cancer

530 participants from 36 countries joined this trial. The map below shows the number of participants who took part in each country.



What treatments did the participants receive?

Researchers used a computer to randomly assign participants to receive either **MBG453** or a **placebo**, both given with **standard treatment**. The treatments in this trial were given in cycles. A **cycle** is a treatment period that is repeated. In this trial, a cycle was 4 weeks. The treatments were:

MBG453 – 800 milligrams (mg) given through a needle in a vein as an intravenous (IV) infusion one time on Day 8 of each cycle.

Placebo – Given as an IV infusion one time on Day 8 of each cycle. It looks like the trial drug but does not have any drug in it.

Standard treatment – Azacitidine 75 mg per square meter of body surface area. It was given as an IV infusion or an injection under the skin on either:

- Days 1-7 of each cycle, or
- Days 1-5, 8, and 9 of each cycle

What is body surface area?

Body surface area is a measure based on a person's height and weight to make sure the person gets the correct dose of treatment for their body size.

The participants, researchers, and trial staff did not know what treatment the participants were receiving. Doing a trial this way helps to make sure that the results are looked at with fairness across all treatments.

Each participant received trial treatment until their cancer got worse, they could not tolerate the treatment, or they or the trial doctor decided to stop treatment.

What happened during this trial?

Before treatment — Up to about 1 month

The trial staff checked to make sure the participants could be in this trial.

During treatment — Up to 3 and a half years

530 participants were randomly assigned to one of these treatments:

- **MBG453 with standard treatment**: 265 participants, and 264 of them received treatment
- **Placebo with standard treatment**: 265 participants, and 264 of them received treatment

2 participants did not receive treatment because their cancer got worse or they decided to leave the trial.

After treatment — Until the trial ended

Trial staff checked participants for any medical problems for up to 5 months after participants' last dose of trial treatment.

Trial staff also called participants to check how long they lived until the end of the trial.

Trial staff checked the participants' general health throughout the trial.

What were the main results of this trial?

Did participants who received MBG453 with standard treatment live longer than those who received placebo with standard treatment?

Participants who received **MBG453 with standard treatment** lived about as long as those who received **placebo with standard treatment**. The researchers concluded the difference between the groups was not meaningful.

To learn this, researchers kept track of the length of time participants lived from when they started the trial until the end of the trial. This is called **overall survival**. They calculated the median overall survival for participants assigned to each trial treatment. **Median overall survival** was the length of time from the start of the trial at which:

- Half of the participants were alive, and
- Half of the participants had died, due to any cause

Length of time participants lived from the start of the trial

The graph below shows the median overall survival of all participants, including participants who were assigned to receive trial treatment but did not receive treatment.

What medical problems, also called adverse events, happened during this trial?

Trial doctors keep track of all medical problems, also called **adverse events**, that happen in trials. They track adverse events even if they think the adverse events are not related to the trial treatments.

Many trials are needed to know if a drug or treatment causes an adverse event.

This section is a summary of the adverse events that happened from the start of treatment until 1 month after their last dose of trial treatment.

An **adverse event** is:

- Any **sign or symptom** that the participants have during a trial
- Considered **serious** when it is life-threatening, causes lasting problems, the participant needs hospital care, or results in death

Adverse events **may** or **may not** be caused by treatments in the trial.

523 out of 528 participants had adverse events, including serious and other (not including serious) adverse events.

- 338 participants had adverse events that were considered serious.
- 84 participants left the trial due to an adverse event.
- 55 participants died

The researchers concluded there were no new safety concerns for **MBG453** in this trial.

One participant assigned to **MBG453 with standard treatment** stopped treatment before receiving **MBG453**. Because they only received **standard treatment**, this participant is included in the **placebo with standard treatment** group in the tables on the next pages.

How many participants had adverse events?

	MBG453 with standard treatment 263 participants	Placebo with standard treatment 265 participants
Had **any adverse event** including serious and other	260 of 263	263 of 265
Had at least 1 **serious adverse event**	174 of 263	164 of 265
Left the trial due to an adverse event	41 of 265	43 of 265
Died	18 of 265	37 of 265

What serious adverse events did the participants have?

338 participants had serious adverse events.

The table below shows the most common serious adverse events.

	MBG453 with standard treatment 263 participants	Placebo with standard treatment 265 participants
Fever and low level of a type of white blood cell Febrile neutropenia	49 of 263 19%	31 of 265 12%
Lung infection Pneumonia	35 of 263 13%	36 of 265 14%
Fever Pyrexia	17 of 263 6%	19 of 265 7%
COVID-19	12 of 263 5%	9 of 265 3%
Low level of red blood cells Anemia	11 of 263 4%	11 of 265 4%
Lower level of platelets Platelet count decreased	10 of 263 4%	7 of 265 3%
Serious complication of an infection Sepsis	3 of 263 1%	10 of 265 4%

What other (not including serious) adverse events did the participants have?

The table below shows the most common other adverse events.

	MBG453 with standard treatment 263 participants	Placebo with standard treatment 265 participants
Trouble passing stool Constipation	141 of 263 54%	114 of 265 43%
Low level of red blood cells Anemia	107 of 263 41%	91 of 265 34%
Low level of a type of white blood cell Neutropenia	96 of 263 37%	76 of 265 29%
Feeling sick to the stomach Nausea	87 of 263 33%	66 of 265 25%
Fever Pyrexia	71 of 263 27%	59 of 265 22%
Low level of platelets Thrombocytopenia	67 of 263 25%	58 of 265 22%

What was learned from this trial?

Researchers learned about the effects of **MBG453** given with standard treatment for people with certain blood cancers. This trial ended early because the results showed that participants with MDS or CMML who received **MBG453 with standard treatment** did not live longer compared to those who received **placebo with standard treatment**. The decision was not due to safety concerns.

The researchers concluded that participants who received **MBG453 with standard treatment** lived about as long as those who received **placebo with standard treatment**. The difference between the groups was not meaningful.

The researchers concluded there were no new safety concerns for **MBG453** in this trial.

When this summary was written, the trial CMBG453B12206B was ongoing to allow participants who were benefiting to continue to receive **MBG453**.

Where can I learn more about this trial?

More information about the results and adverse events in this trial can be found in the scientific summary of the results available on the Novartis Clinical Trial Results website **www.novctrd.com**

Follow these steps to find the scientific summary:

Go to **www.novctrd.com** → Click **Clinical Trial Results** → Accept the terms **I accept** → Search by study number **CMBG453B12301**

For more information about this trial, go to any of these websites:

- **clinicaltrials.gov** – search using the number **NCT04266301**
- **clinicaltrialsregister.eu** – search using the number **2019-002089-11**

Other trials of **MBG453** may appear on the public websites above. When there, search for **MBG453** or sabatolimab.

Full clinical trial title: A randomized, double-blind, placebo-controlled phase III multi-center study of azacitidine with or without MBG453 for the treatment of patients with intermediate, high or very high risk myelodysplastic syndrome (MDS) as per IPSS-R, or Chronic Myelomonocytic Leukemia-2 (CMML-2)

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1-888-669-6682 (US) | +41-61-324 1111 (EU)

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